Remarks

Further and favorable reconsideration is respectfully requested in view of the foregoing amendments and following remarks.

Initially, the cross reference to the parent applications previously inserted by Preliminary Amendment has been amended to indicate the patented status of the immediate parent application, Serial No. 10/143,962.

Claim 10 has been amended to recite that the film effects the transmucosal delivery of the pharmaceutically active agent(s) when adhered to the oral cavity, which is based on the disclosure in the paragraph bridging pages 5 and 6 of the specification as filed.

Claim 28 has been to limit the composition to a film that is orally applicable and has a thickness of not more than 70 μm, which is based on the disclosure at page 7, line 21.

Accordingly, claim 29, which is dependent on claim 28, has been amended to recite that the thickness of the film is between 5 and 70 μm.

The patentability of the presently claimed invention over the disclosures of the references relied upon by the Examiner in rejecting the claims will be apparent upon consideration of the following remarks.

Thus, the rejection of claims 28-29, 31, 33-35 and 38 under 35 U.S.C. §102(b) as being anticipated by Keith et al. (US 4,764,378) is respectfully traversed.

Claim 28, as presently amended, requires the thickness of the film to be not more than 70 μm. Keith et al. disclose dosage forms having a thickness in the range of 0.2 to 3 mm (col. 6, lines 1-9), i.e. 200-3000 μm. According to the present specification (page 7, lines 19-21), a dry film thickness of 70 μm should not be exceeded in order to avoid an adverse feeling in the mouth. Keith et al. do not disclose dosage forms having a thickness of less than 0.2 mm (less than 200 μm). Hence, the compositions defined in claim 28, as now amended, are novel over this reference.

The same applies to claims 29, 31, 33-35 and 38, which are dependent on claim 28.

The rejection of claims 10 and 13 under 35 U.S.C. §103(a) as being unpatentable over Schmidt (US 5,354,551) is respectfully traversed.

This reference relates to a mouth and tooth care preparation. Although this preparation is described as being present in the form of a film, it is not described as being mucoadhesive. In fact, since this preparation is used similarly as a toothpaste, mucoadhesiveness would interfere with its intended use (see col. 1, lines 8-56; and col. 3, lines 2-10). If the mouth and tooth care preparation disclosed by Schmidt was mucoadhesive, this would cause the preparation (or the particles resulting from its degradation) to stick to the oral mucosa, e.g. the tongue, which is clearly not desirable but rather should be avoided in accordance with Schmidt's teaching.

Furthermore, the Examiner has suggested that Schmidt would teach active agents. In this connection, the monolayer films of the present invention are designed to provide transmucosal delivery of the active agents that are incorporated in the matrix of the film. Upon transmucosal delivery, the active agents become systemically available and may then be therapeutically effective in various organs or tissues of the body (see examples of therapeutic agents mentioned in the paragraph bridging pages 5 and 6 of the present specification). As noted by the Examiner, Schmidt mentions "antibacterial agents" (col. 2, line 25) that may be added to the mouth and tooth care preparations. However, these antibacterial agents have the same effect as any antibacterial agents present in toothpastes or mouth rinses. These agents (e.g. chlorhexidine) are added to provide local antibacterial action exclusively in the oral cavity, without being absorbed by the oral mucosa. Therefore, the skilled person desiring to make an oral composition for transmucosal delivery of active substances would never have considered the teaching by Schmidt which relates to mouth and tooth care preparations. Schmidt does not indicate that the mouth and tooth care preparations are suitable for effecting transmucosal delivery of the "antibacterial agents".

The rejection of claim 19 under 35 U.S.C. §103(a) as being unpatentable over Schmidt in view of Story et al. (US 4,944,949) is respectfully traversed.

Applicants' comments set forth above with regard to the Schmidt reference are equally applicable to this rejection.

Story et al. was cited for teaching the presence of a second or further surfactant. This document discloses non-steroidal anti-inflammatory drugs (NSAIDs) which are formulated with surfactants to give micelle-forming compositions (see Abstract). Hence, the formation of these compositions critically depends on the presence of a particular type of drug (NSAID) and surfactants that are capable of forming micelles when combined with these particular drug substances. According to the teaching of Story et al., the surfactant is not merely used "to dissolve the drug" (as suggested by the Examiner), but is used in order to allow micelle formation.

Furthermore, since Schmidt does not refer to NSAIDs, there would have been no motivation to combine Story et al. with Schmidt. It is unknown whether any of the "additives" mentioned by Schmidt would be suitable for micelle formation as taught by Story et al. According to Schmidt, the "tensides" (surfactants) were added as "foaming agents" (col. 2, lines 10-12); and Applicants note that foaming agents are frequently used in mouth and tooth care preparations. However, Schmidt does not suggest that the tensides would have any effect on the dispersion of a pharmaceutically active agent that might be present in the preparation. Therefore, the incorporation of surfactants as taught by Schmidt serves a completely different purpose as compared to the incorporation of surfactants as taught by Story et al.

Applicants also point out that Schmidt, as discussed above, does not pertain to mucoadhesive compositions that are capable of transmucosal administration of drug substances, but instead pertains to mouth and tooth care preparations that are not designed for transmucosal drug delivery. Therefore, Schmidt pertains to a field of technology that is quite different from the subject matter disclosed by Story et al., as well as from the present invention.

The rejection of claims 11-12, 14-18 and 21-23 under U.S.C. §103(a) as being unpatentable over Schmidt in view of Acharya (US 5,686,094) is respectfully traversed.

Acharya was cited for teaching flavor enhancers, colorants and particular sweeteners such as aspartame and sorbitol.

Claims 11, 12, 14-18 and 21-23 are dependent on claim 10 which has now been amended. Therefore, the arguments presented above with respect to Schmidt are equally applicable to the rejection of these dependent claims.

Additionally, the mouth and tooth care preparations described by Schmidt are not described as compositions for release of an active agent to the oral mucosa. On the other hand, Acharya does not relate to mouth and tooth care preparations (that are intended to be used for hygienic purposes rather than for therapeutic treatment), but relates to drug delivery systems. Therefore, it would not have been obvious to use the additives mentioned by Acharya as being suitable for use in a drug delivery system, in the mouth and tooth care preparation disclosed by Schmidt.

The rejection of claims 24-27 and 32 under U.S.C. §103(a) as being unpatentable over Keith et al. in view of Acharya is respectfully traversed.

Keith et al. disclose mucoadhesive buccal dosage forms for transmucosal administration of, e.g. nicotine. However, although this reference mentions (col. 4, lines 28-31) that minor amounts of additional ingredients may be incorporated, these ingredients are not specified. These ingredients are added to modify the physical properties of the matrix. Plasticizers are mentioned as an example of "additional ingredients"; clearly, plasticizers have the sole effect of modifying the physical properties of the polymer matrix. Keith et al. do not provide any motivation for adding any "additional ingredients" that have other functions, e.g. flavoring agents, sweeteners, or tartaric acid (present claim 24). Therefore, based on the teaching provided by Keith et al., there would not seem to have been any motivation to combine this reference with Acharya, which relates to delivery systems tor delivering active agents to the oral mucosa (col. 3, lines 12-27). Nicotine is not mentioned as a suitable active substance. The flavors, sweeteners, etc. disclosed by Acharya were not described as being suitable for being used in combination with nicotine. Nicotine is a substance having an unpleasant odor and a sharp, burning taste. Since Keith et al. fail to mention any flavoring substances, sweeteners and flavor enhancing agents at all, and since Acharya does not consider the use of nicotine as an active substance, it would not have been obvious for a skilled person to combine nicotine or a nicotine salt, in a mucoadhesive monolayer film, with flavoring agents, sweeteners and tartaric acid, as defined in present claim 24.

Claim 32 is dependent on claim 28 which has now been amended by limiting the film thickness to not more than 70 μm. According to Keith et al., the dosage forms may have a thickness in the range of 0.2 to 3 mm (col. 6, lines 2-7) as indicated above, which

is considerably higher than 70 μm. As also indicated above, and as explained in the present specification (page 7, lines 19-21), a dry film thickness of 70 μm should not be exceeded to reliably avoid an adverse feeling in the mouth.

The rejection of claims 28, 30 and 39-40 under 35 U.S.C. §103(a) as being unpatentable over Keith et al. in view of Stanley et al. (US 5,783,207) is respectfully traversed.

Claims 30 and 39-40 are dependent on claim 28 which has now been amended by limiting the film thickness to not more than 70 μm which is below the range indicated by Keith et al. Stanley et al. likewise fails to disclose nicotine-containing films having a thickness of not more than 70 μm. Therefore, nicotine-containing films having such thickness were not rendered obvious by the combined disclosure of Keith et al. and Stanley et al.

The rejection of claims 20 and 36-37 under U.S.C. §103(a) as being unpatentable over Keith et al. in view of Story et al. is respectfully traversed.

As noted above, Keith et al. merely mention the possibility of adding additional ingredients for modifying the physical properties of the matrix, but do not teach incorporating surfactants. On the other hand, Story et al. mention surfactants, but not in combination with nicotine. The teaching of Story et al. is only concerned with NSAIDs, and the surfactants are added to give micelle-forming compositions. There was no motivation for a skilled person to modify Keith et al. to obtain a micelle-forming composition. In addition, since micelle-forming compositions are described by Keith et al. only in connection with NSAIDs, it would not have been obvious that micelle-forming compositions could be obtained when nicotine is used as the active ingredient, instead of NSAIDs. Since the addition of surfactants according to Keith et al. is mentioned specifically in connection with micelle formation in the presence of NSAIDs, it is apparent that one skilled in the art would not have used the surfactants and mixtures thereof disclosed by Story et al. in the buccal dosage forms taught by Keith et al.

In response to the four obviousness-type double patenting rejections as set forth on pages 12-15 of the Office Action, Applicants are submitting herewith a Terminal Disclaimer, which will be effective to overcome all of these double patenting rejections.

In view of the foregoing amendments and remarks, it is submitted that each of the grounds of rejection set forth by the Examiner has been overcome, and that the application is in condition for allowance. Such allowance is solicited.

Respectfully submitted,

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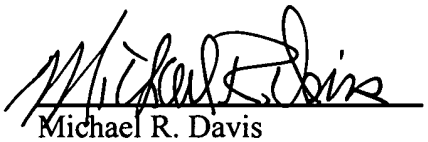
By: 

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October 16, 2006